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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,229	10/10/2003	Lin Zhi	45026.00128.UTL1	8639

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EXAMINER	
AULAKH, CHARANJIT	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/684,229	ZHI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	-

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-43 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8,14,17-24 and 28-43 is/are rejected.

7)☒ Claim(s) 9-13,15,16 and 25-27 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-43 are pending in the application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 14, 17 and 28-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858. F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed: Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, the state of the prior art, presence of working examples and the breadth of claims.

The instant compounds are agonist at progesterone receptor as shown by data in tables 1 and 2 on pages 67-68. It is of note that most of the exemplified compounds showed

only agonist activity at progesterone receptor (see tables 1 and 2). Therefore, based on this data, the instant compounds will have utility in treating disease conditions where progesterone receptor agonists are well known in the prior art to have therapeutic effect. There is no teaching either in the specification or prior art references showing therapeutic effect of progesterone receptor agonists. There are no working examples present showing efficacy of instant compounds in known animal models of any disease conditions where progesterone receptor agonist activity is implicated in their etiology. The instant compounds of formula (I) encompasses several hundreds of thousands of compounds based on the values of variables R1-R21 and n and therefore, in absence of such teachings, guidance and working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of all disease conditions where progesterone receptor agonist activity is implicated in their etiology.

It is well known in the art that the efficacy of a prodrug following in vivo administration depends upon release of parent compound to its target in vivo. A prodrug of any compound does not necessarily mean that the parent compound will be released in vivo since it is influenced by various factors such as absorption, metabolism, degradation by esterases etc. It is of note that there is not even a single example present in the specification of any prodrug. As stated earlier, the instant compounds of formula (I) encompass several hundreds of thousands of compounds based on the values of various variables and therefore, in absence of such teachings, guidance and working examples, it would require undue experimentation to prepare different

prodrugs of all compounds encompassed by instant formula (I) which will be effective in releasing parent compound to its target following their in vivo administration.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 14, 17, 28-30, 33, 35, 41 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 14, 17, 29 and 30, the term ---prodrug--- is indefinite since specific prodrugs and a method of preparing them are not defined.

In claims 28-30, the term ---condition mediated by a progesterone receptor --- is indefinite since specific conditions are not defined and furthermore, it is not clear whether these conditions are mediated by either hyperactivity or hypoactivity of progesterone receptor.

In claims 33 and 35, the term ---modulating----is indefinite since it is not clear whether it is directed to increased or decreased fertility or activity of progesterone receptor. In claim 41, the type of cancer to be treated is not defined.

In claim 43, it is not clear whether the method is directed to in vitro or in vivo method and furthermore, the steps for testing the contracted cell to determine the presence of progesterone receptor are missing. Also, it is not clear what is being used to label the compounds?

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-8, 17-24 and 28-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhi (J. Med. Chem., cited on applicants form 1449).

Zhi discloses 5-aryl-1,2-dihydrochromeno[3,4-f]quinolines as progesterone receptor agonists. The compounds 13-32 (see chart 2 on page 293) disclosed by Zhi anticipate the instant claims when R13 and R14 together form a bond, R16 and R18 together form a bond and R20 and R21 together form a bond to make phenyl ring when n is 1 in the instant compounds of formula (I).

Allowable Subject Matter

7. Claims 9-13, 15, 16 and 25-27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The compounds of instant claims are neither disclosed nor obvious over the prior art. In the prior art, Coghlan (WO 02/02565, cited on applicants form 1449) discloses compounds of formula I as glucocorticoid-selective anti-inflammatory agents which are closely related to instant compounds. However, the closely related compounds disclosed in examples 131, 133, 136, 137, 140-144, 146, 148-150, 152-170, 209, 212, 220-222, 224, 225, 236-243, 246, 247, 252, 253, 263-265 and 270-273 by Coghlan differ from the instant compounds in having methoxy or halogen substituted at position 10 instead of H in the instant compounds of formula (I).

8. Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625